Accepted Manuscript

Title: Do endometriomas grow during ovarian stimulation for assisted reproduction? a three-dimensional volume analysis before and after ovarian stimulation

Author: Ayse Seyhan, Bulent Urman, Engin Turkgeldi, Baris Ata

PII: S1472-6483(17)30610-7
DOI: https://doi.org/10.1016/j.rbmo.2017.10.108
Reference: RBMO 1842

To appear in: *Reproductive BioMedicine Online*

Received date: 8-7-2017
Revised date: 18-10-2017
Accepted date: 20-10-2017

Please cite this article as: Ayse Seyhan, Bulent Urman, Engin Turkgeldi, Baris Ata, Do endometriomas grow during ovarian stimulation for assisted reproduction? a three-dimensional volume analysis before and after ovarian stimulation, *Reproductive BioMedicine Online* (2017), https://doi.org/10.1016/j.rbmo.2017.10.108.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

ACCEPTED MANUSCRIPT

Short title: Endometrioma volume in IVF

Do endometriomas grow during ovarian stimulation for assisted reproduction? A three-dimensional volume analysis before and after ovarian stimulation

Ayse Seyhan,[a] Bulent Urman,[a,b] Engin Turkgeldi,[c] Baris Ata,[b,*]

[a]Assisted Reproduction Unit of the American Hospital of Istanbul, Istanbul, Turkey
[b]Department of Obstetrics and Gynecology, Koc University School of Medicine, Istanbul, Turkey
[c]Department of Obstetrics and Gynecology, Koc University Hospital, Davutpasa Caddesi No: 4, Topkapi, 34010, Istanbul, Turkey

*Corresponding author: Baris ATA, MD, The Assisted Reproduction Unit, Koc University Hospital, Davutpasa Caddesi No: 4, Topkapi, 34010, Istanbul, Turkey. Tel: +90 212 850 2 850; E-mail address: barisata@ku.edu.tr

Comment [MD1]: Author: please provide full postal addresses for addresses a and b.

Accepted Manuscript

Key message

Endometrioma volume significantly increased during ovarian stimulation for assisted reproduction techniques; however, the absolute increase is small and possibly transient and clinically insignificant.

Abstract

Whether endometriomas grow because of supraphysiological oestradiol levels attained during ovarian stimulation for assisted reproduction techniques is a concern. In this prospective study, 25 women with 28 endometriomas underwent three-dimensional ultrasound using sono-automated volume calculation software. Endometrioma volume was measured on the first day of gonadotrophin injection (V1) and the day of ovulation trigger (V2). Nine (36%) women were stimulated in a gonadotrophin releasing hormone antagonist protocol (GnRH), 13 (52%) in a long, and three (12%) in an ultra-long GnRH agonist protocol. Mean duration

ACCEPTED MANUSCRIPT

of stimulation was 10.3 days with median total gonadotrophin dose of 4500 IU/day. Median number of cumulus oocyte complexes was five, and metaphase-two oocytes was four. None of the endometriomas were punctured during oocyte retrieval. Median V1 was 22.2 ml (12–30 ml) and median V2 was 24.99 ml (11.2–37.4 ml) with $P = 0.001$. Twenty-three out of 28 endometriomas (82%) grew to some extent during ovarian stimulation. Endometrioma growth was positively correlated with prestimulation cyst volume (Correlation coefficient 0.664; $P < 0.01$). Although the 3-ml average growth was statistically significant, it could be regarded as clinically insignificant.

KEYWORDS: endometrioma, endometriosis, IVF, ovarian stimulation, three-dimensional ultrasound, volume

Author biography

Ayse Seyhan graduated from the Istanbul School of Medicine. After residency training in Obstetrics and Gynaecology, she completed a clinical fellowship in ultrasound in reproductive medicine at the McGill University Reproductive Center between 2010 and 2012. Her research is focused on clinical aspects of assisted reproduction.

<A>Introduction

Endometriosis is a chronic condition that is characterized by the presence of endometrial glands and stroma outside the uterine cavity. Ovarian endometriotic cysts are present in about 20–40% women with endometriosis (Redwine, 1999; Vercellini *et al*., 2003). Endometriosis is associated with subfertility, and endometrioma is often diagnosed during infertility work-up. Many women with ovarian endometriomas will eventually undergo an assisted reproduction technique cycle for endometriosis-associated infertility or for other indications. Optimal management of endometrioma before an assisted reproduction technique cycle, however, is controversial. Current evidence supports a conservative approach, as the presence of an endometrioma does not decrease live birth rates (Hamdan *et al*., 2015). Moreover, surgical excision, rather than being beneficial, may adversely affect ovarian reserve thereby

Accepted Manuscript

ACCEPTED MANUSCRIPT

decreasing the number of collected oocytes (Hamdan *et al*., 2015). As a result, many women with endometriomas undergo an assisted reproduction technique cycle without surgical excision.

Endometriosis is an oestrogen-dependent condition. Oestrogen stimulates the growth of ectopic endometriotic foci, and supraphysiological oestradiol levels associated with ovarian stimulation could possibly lead to their growth (Garcia-Velasco and Somigliana, 2009). Previously published studies with conventional two-dimensional ultrasound reported that endometrioma size remained unchanged after ovarian stimulation for assisted reproduction techniques (Benaglia *et al*., 2009; 2011). Two-dimensional ultrasound measurements of ovarian follicles have notoriously poor accuracy and reproducibility, especially in the presence of multi-follicular growth in assisted reproduction technique cycles (Ata and Tulandi, 2011). Similar limitations can be anticipated in the assessment of endometriomas within stimulated ovaries. Three-dimensional ultrasound technology and automatic volume calculation software (SonoAVC) accurately measure ovarian structures with less inter- and intra-observer variation than conventional two-dimensional ultrasound (Ata and Tulandi, 2011). The aim of the present study was to determine whether ovarian stimulation is associated with an increase in endometrioma volume as measured by SonoAVC.

Accepted Manuscript

ACCEPTED MANUSCRIPT

<A>Material and methods

This prospective study was conducted in the Assisted Reproduction Center of the American Hospital of Istanbul, between April 2015 and March 2016. Koc University Clinical Research Ethics Committee approved the study protocol on December 26, 2014 (reference number: 2014.199.IRB1.013), and all participants provided written informed consent. All women who were due to start ovarian stimulation for assisted reproduction techniques were eligible for participation if they had at least one endometrioma. An endometrioma was defined by the visualization of an ovarian cyst with regular margins and ground-glass echogenicity on transvaginal ultrasound examination. The presence of the cyst was confirmed at least on two separate examinations carried out at least one month apart to rule out other haemorrhagic cysts that could be confused with an endometrioma (Savelli, 2009; Exacoustos *et al*., 2014).

Ovarian stimulation protocols are defined elsewhere (Ata *et al*., 2017). Briefly, the long gonadotrophin releasing hormone (GnRH) agonist involved daily subcutaneous injections of 0.5 mg leuprolide acetate (Lucrin Daily, Abbot), starting from the mid-luteal phase of the preceding cycle until the day of ovulation trigger. The GnRH antagonist protocol involved daily subcutaneous injection of 0.25 mg cetrorelix acetate (Cetrotide, MerckSerono) starting from the sixth day of ovarian stimulation until the day of ovulation trigger. Gonadotrophin injections were started on the second or third day of menstrual bleeding, and daily dosage ranged between 150 and 450 IU at the physician's discretion. When two or more follicles reached 18 mm or over in diameter, 250 µg recombinant HCG (Ovitrelle, MerckSerono) was administered to be followed by transvaginal oocyte retrieval 36 h later. In patients who underwent an embryo transfer, one or two embryos were transferred on day 3 or 5 using a Wallace or Cook catheter.

<B>Assessment of endometrioma volume

Accepted Manuscript

ACCEPTED MANUSCRIPT

Participants underwent two- and three-dimensional ultrasound monitoring of ovarian stimulation with a Voluson E8 using SonoAVC software (General Electric, Kratz, Austria). A single investigator (AS) conducted all scans with a 5–9 mHz intravaginal probe. Endometrioma volume was measured on the first day of gonadotrophin injection (V1) and the day of ovulation trigger (V2).

A three-dimensional volume of each ovary was captured without taking any automated measurements. Raw ovarian volumes were labelled with an identification number and stored. One month after completion of data collection, the ovarian volumes were analysed with SonoAVC in random order to prevent remembering the participants and the day of measurements, i.e. V1 or V2. SonoAVC automatically analyses the captured volume in voxels, i.e. three-dimensional equivalent of two-dimensional pixel, and checks for differences between echogenicity of adjacent voxels. When the difference between the echogenicity of two adjacent voxels exceeds a predefined threshold, they are identified as separate structures by the software. Thus, hypoechogenic follicles within the captured ovarian volume are identified and a set of measurements are generated for each follicle. The volume calculation is based on the voxel count within the identified follicle. Mean follicular diameter (MFD) is the arithmetic mean of the three longest orthogonal diameters.

SonoAVC provides post-processing options. Briefly, any follicles that are overlooked by the software can be added to, and any hypoechoic regions, such as free fluid around the ovaries or blood vessels adjacent to the ovaries, which could be erroneously included in the follicle count, can be excluded from the follicle count by simply using the ‘add/remove’ function. The ‘cut’ function is used to separate any adjacent follicles with thin follicular walls, which could have been erroneously identified and measured as a single follicle by the software, and to trim follicular borders to fit to the exact shape of the follicle. Rarely, a single follicle with heterogenous echogenicity can be identified as separate follicles by the software, and the

Accepted Manuscript

ACCEPTED MANUSCRIPT

'merge' function is used to combine them to be counted as a single follicle. The settings of growth and separation within the software were kept uniform at default values of 'mid' for all follicle measurements.

Although SonoAVC is developed for follicle measurements, the unique echogenicity of endometriomas differ from both ovarian follicles and ovarian tissue, and therefore enable their identification as separate structures by SonoAVC (**Figure 1**). In the case of incomplete identification, endometrioma borders can be precisely marked by using the above mentioned post-processing options.

<B>Statistical considerations and sample size calculation

Continuous variables were defined with mean (SD) or median (25th to 75th percentile), depending on the distribution characteristics. Categorical variables were defined with numbers and percentages. Matched pairs Wilcoxon Signed Rank test was used to compare endometrioma volumes and mean diameters at the start and end of stimulation. Spearman's rho was calculated for bivariate correlation analyses. A two-sided *P*-value less than 0.05 was considered statistically significant.

The mean endometrioma diameter was about 4 cm in our previous studies on endometrioma excision (Uncu *et al*., 2013; Urman *et al*., 2013). We assumed women undergoing assisted reproduction techniques without prior surgical excision would have smaller cysts, e.g. on average 3 cm in diameter. We supposed a minimum change of 1 cm would enable reliably attributing the change to true growth of the cyst rather than measurement variation. A 1-cm increase in diameter over 3 cm corresponds to 19 ml increase in cyst volume (to 33.5 ml from 14.3 ml). Several sample size calculations for repeated measures (matched pairs t-test or matched pairs Wilcoxon signed rank tests) with different assumptions for mean cyst volumes and standard deviations (SD) (V1 ranging between 4 and 14 ml with SDs between 2 and 16,

Accepted Manuscript

ACCEPTED MANUSCRIPT

V2 ranging between 14 ml and 34 ml, with SDs between 7 and 19 ml) for a significance level of 0.05 and power of 0.8 yielded required minimum sample sizes between 2 and 14. Anticipating possible deviations from our assumptions, we arbitrarily decided to recruit 25 women. G*Power 3.1 (www.gpower.hhu.de) was used from sample size calculations.

Accepted Manuscript

ACCEPTED MANUSCRIPT

<A>Results

Twenty-five women with 28 endometriomas were recruited between January and December 2015. The mean age of participants was 36.1 ± 4.6 years (range 27–43 years). Median body mass index (25th to 75th percentile) was 22.9 (19.3–25.7) kg/m^2. Indications for assisted reproduction techniques was poor ovarian reserve in 14, endometriosis alone in seven, tubal factor in two, male factor in one and fertility preservation in one woman. Four patients had bilateral endometriomas and three of them had a history of a prior endometrioma excision. Median total antral follicle count was 5 (3–8), and median serum anti-Müllerian hormone level was 1.11 (0.7–1.83) ng/ml.

Nine (36%) women were stimulated in a GnRH antagonist cycle, 13 (52%) in long GnRH agonist protocol, and three (12%) ultra-long protocol. Mean duration of stimulation was 10.3 (2.3) days with median total gonadotrophin dose of 4500 (3113–4950) IU. Median number of follicles wider than 14 mm was four (two to seven), median peak oestradiol level 1200 (821–2300) pg/ml, number of cumulus oocyte complexes was five (four to nine), and metaphase-two oocytes was four (three to seven). None of the endometriomas were punctured during oocyte retrieval. No new endometriomas were detected at the end of the stimulation.

Median V1 was 22.2 ml (12–30 ml) and median V2 was 24.99 ml (11.2–37.4 ml); $P = 0.001$. Twenty-three out of 28 endometriomas (82%) grew to some extent after ovarian stimulation.

The results were similar when the mean diameter reported as MFD by SonoAVC was used as the surrogate of endometrioma size. Median MFD was 37.5 (29.5– 40.7) mm on the first day of stimulation, and 40.5 (30.4–43.5) mm on the last day of stimulation ($P < 0.01$).

Endometrioma growth was positively correlated with the prestimulation volume of the cysts (V1) (Spearman's correlation coefficient 0.664; $P < 0.01$). Larger cysts grew more during

ACCEPTED MANUSCRIPT

stimulation (**Figure 2**). Measures of ovarian response, i.e. number of follicles wider than 14 mm, total number of cumulus oocyte complexes, and serum oestradiol level on the day of trigger, were not significantly correlated with change in endometrioma volume. Moreover, there was a trend towards negative correlation between change in endometrioma volume and ovarian response (**Table 1**).

Fourteen patients underwent fresh embryo transfer. One patient underwent oocyte cryopreservation for fertility preservation. Nine patients had total embryo cryopreservation, six for embryo pooling, one because of an endometrial polyp diagnosed during ovarian stimulation, one from pending ovarian hyperstimulation syndrome, and one from detection of a hydrosalpinx during ovarian stimulation. One patient's cycle was cancelled owing to fertilization failure. Overall embryo implantation rate per fresh embryo transfer was 28.6% (6/21). Live birth rate per fresh embryo transfer was 42.8% (6/14). Baseline characteristics and assisted reproduction technique outcome parameters are presented in **Table 2**.

Accepted Manuscript

ACCEPTED MANUSCRIPT

<A>Discussion

Our results demonstrate that most endometriomas grow to some extent during ovarian stimulation.

The lack of a histologic diagnosis of endometriomas can be regarded as a limitation of the present study. As surgical excision is associated with a further decrease in ovarian reserve and does not seem to improve assisted reproduction technique outcome (Somigliana *et al*., 2012; Ata and Uncu, 2015; Hamdan *et al*., 2015; Ata *et al*., 2017), current indications for surgery are rather limited. These include pain unresponsive to medical treatment, organ involvement, e.g. hydronephrosis, spontaneous rupture of endometrioma or strong suspicion of malignancy. Currently, transvaginal ultrasound is the mainstay for the diagnosis of endometriomas. In a recent Cochrane review, transvaginal ultrasound was found to have sensitivity of 0.93 (95% CI 0.87 to 0.99) and specificity 0.96 (95% CI 0.92 to 0.99) for diagnosing endometriomas. Therefore, transvaginal ultrasound qualified as a SpPin triage test and approached the criteria for a SnNout triage test (Nisenblat *et al*., 2016). Finally, all the scans in this study were carried out by a single physician (AS) with vast experience in reproductive ultrasound, with more than 5000 scans to her credit. Moreover, saved ovarian volumes and SonoAVC markings were reviewed by a second observer (BA). Therefore, we deem it unlikely to have included other cysts besides endometriomas in the present analysis.

Two other studies, using two-dimensional ultrasound prospectively evaluated the effect of ovarian stimulation on the growth of preexisting endometriomas (Benaglia *et al*., 2009; 2011). Benaglia *et al*. (2009) compared the size of 70 endometriomas in 48 women, between the month preceding ovarian stimulation for assisted reproduction technique and 3–6 months after completion of treatment. They calculated endometrioma volume using the collate ellipsoid

ACCEPTED MANUSCRIPT

formula, i.e. by multiplying the three orthogonal diameters of the cyst by $\pi/6$. The median (interquartile range [IQR]) volume was 3.9 (2.9–7.9) and 4.9 (2.4–9.9) ml, before and after assisted reproduction techniques, respectively. The difference was not found to be statistically significant. The median diameter (interquartile range) before assisted reproduction techniques was 20 (16–25) mm. Thirty-five women with 45 endometriomas were included in the second study by the same group (Benaglia *et al*., 2011). The first and the second assessment were at the same time points as in the previous study. They compared the mean of three orthogonal diameters, rather than volume, and median (IQR) diameter was 20 (12–27) and 20 (17–27) mm, before and after assisted reproduction techniques. As with the previous study, the difference was not significant. Women who conceived were excluded from the comparisons in both studies. There could be several explanations for the discrepancy between our observations and those of Benaglia *et al*. First, the endometriomas in our study were bigger; the median endometrioma volume before stimulation was 3.9 ml in the first study by Benaglia *et al* (2009), whereas, it was 22 ml in ours. The median cyst diameter was 37 mm in our study compared with 20 mm in both aforementioned studies (Benaglia *et al*., 2009; 2011). Even if endometriomas grow in response to supraphysiologic oestrogen levels during assisted reproduction techniques, the difference can be too small to detect a significant growth when serial measurements are taken in smaller cyst sizes. Indeed, the cysts tended to grow in both previously published studies. The median volume increased from 3.9 ml to 4.9 ml in the first study by Benaglia *et al*. (2009). Similarly, the 25th percentile value for the diameter increased from 12 to 17 mm in the latter series (Benaglia *et al*., 2011). Although Benaglia *et al*. concluded that cyst growth was not related to initial cyst size, with subgroup analysis based on cyst size before and after stimulation, we observed a significant positive correlation between prestimulation cyst volume and absolute growth. Despite having a larger sample size than the present study, their samples could have been inadequate to demonstrate the observed

Accepted Manuscript

ACCEPTED MANUSCRIPT

small absolute differences as statistically significant. Second, the sonographers conducting the second measurement were not blinded for the study design in the previously published studies (Benaglia *et al.*, 2009; 2011). Therefore, there was a small risk that the two-dimensional measurements, which have substantial inter and intra-rater variation, could have been unconsciously affected on the basis of the observers' expectations. We aimed to minimize this risk by conducting automated volume measurements, which have lower inter and intra-rater variation than two-dimensional measurements, and by taking the measurements on anonymized ovarian volumes on a later date (Ata and Tulandi, 2011). Last, but not the least, the different timing of post-stimulation assessment could have caused the discrepancy. Although we measured the cysts on the HCG trigger day, post-stimulation assessments were carried out 3–6 months later in both previous studies. Spontaneous growth of endometriomas is possible during the period of 3–6 months, i.e. overestimating effect of stimulation; however, endometriomas could have shrunk during the same period after an initial growth during stimulation (underestimating effect of stimulation). We were unable to conduct a third measurement 3–6 months after stimulation on most of our patients for a number of reasons, including being from out of town, changing treatment centre and becoming pregnant. These differences prevent direct comparison of our results with prior studies.

Endometrioma growth could have been affected by the choice of stimulation protocol. Arguably, endometriomas could have initially shrunk under ultra/long GnRH agonist protocols and then returned to the original size with ovarian stimulation. If this was the case, one could expect endometrioma size to remain unchanged under GnRH antagonist protocols, as they would not have shrunk before ovarian stimulation. When women who underwent assisted reproduction techniques in a GnRH antagonist cycle were analysed separately, they had median V1 of 19.1 ml (11.7– 6.6 ml) and V2 of 24.90 ml (12.6–43.9 ml), with $P = 0.003$, indicating significant growth despite the absence of a theoretical shrinkage before stimulation.

ACCEPTED MANUSCRIPT

Endometrioma growth not being correlated with ovarian response, and the tendency towards a negative correlation between the two, seems counterintuitive at first glance. When regarded together with the significant positive correlation between prestimulation cyst size and change in endometrioma volume, however, it could be argued that larger cysts, possibly harbouring active endometriotic foci, could tend to suppress ovarian response as they grow further under stimulation. Although our study was adequately powered to detect small changes in endometrioma volume, other studies would be needed to confirm or refute the results of the correlation analyses.

Although our three-dimensional volume measurements suggest that ovarian stimulation causes a statistically significant growth in endometrioma size, and growth is proportionate with prestimulation cyst size, absolute growth seems clinically insignificant and perhaps transient based on the results of Benaglia *et al*. (2009; 2011). Our reassuring findings from larger cysts are perhaps clinically more relevant today than in 2005–2008, when women were recruited for the previously published studies (Benaglia *et al*., 2009; 2011). This is because the excision of endometriomas over 3–4 cm was almost the norm back then, whereas today cyst size *per se* is usually not regarded as an indication for surgery, except for large cysts, i.e. 10 cm or over.

In conclusion, despite a statistically significant increase in endometrioma volume at the end of ovarian stimulation for assisted reproduction techniques, the absolute increase is likely to be clinically insignificant and may even be transient.

Accepted Manuscript

ACCEPTED MANUSCRIPT

References

Ata B, Mumusoglu S, Aslan K, Seyhan A, Kasapoglu I, Avci B, Urman B, Bozdag G, Uncu G. Which is worse? Comparison of ART outcome between women with primary or recurrent endometriomas. *Hum Reprod* 2017: 1-5.

Ata B, Tulandi T. Ultrasound automated volume calculation in reproduction and in pregnancy. *Fertil Steril* 2011;**95**: 2163-2170.

Ata B, Uncu G. Impact of endometriomas and their removal on ovarian reserve. *Curr Opin Obstet Gynecol* 2015;**27**: 235-241.

Benaglia L, Somigliana E, Santi G, Scarduelli C, Ragni G, Fedele L. IVF and endometriosis-related symptom progression: insights from a prospective study. *Human reproduction* 2011;**26**: 2368-2372.

Benaglia L, Somigliana E, Vighi V, Nicolosi AE, Iemmello R, Ragni G. Is the dimension of ovarian endometriomas significantly modified by IVF-ICSI cycles? *Reproductive biomedicine online* 2009;**18**: 401-406.

Exacoustos C, Manganaro L, Zupi E. Imaging for the evaluation of endometriosis and adenomyosis. *Best Pract Res Clin Obstet Gynaecol* 2014;**28**: 655-681.

Garcia-Velasco JA, Somigliana E. Management of endometriomas in women requiring IVF: to touch or not to touch. *Hum Reprod* 2009;**24**: 496-501.

Hamdan M, Dunselman G, Li TC, Cheong Y. The impact of endometrioma on IVF/ICSI outcomes: a systematic review and meta-analysis. *Hum Reprod Update* 2015;**21**: 809-825.

Nisenblat V, Bossuyt PM, Farquhar C, Johnson N, Hull ML. Imaging modalities for the non-invasive diagnosis of endometriosis. Cochrane Database Syst Rev 2016;2: CD009591.

Redwine DB. Ovarian endometriosis: a marker for more extensive pelvic and intestinal disease. *Fertil Steril* 1999;**72**: 310-315.

Accepted Manuscript

ACCEPTED MANUSCRIPT

Savelli L. Transvaginal sonography for the assessment of ovarian and pelvic endometriosis: how deep is our understanding? *Ultrasound Obstet Gynecol* 2009;**33**: 497-501.

Somigliana E, Berlanda N, Benaglia L, Vigano P, Vercellini P, Fedele L. Surgical excision of endometriomas and ovarian reserve: a systematic review on serum antimullerian hormone level modifications. *Fertil Steril* 2012;**98**: 1531-1538.

Uncu G, Kasapoglu I, Ozerkan K, Seyhan A, Oral Yilmaztepe A, Ata B. Prospective assessment of the impact of endometriomas and their removal on ovarian reserve and determinants of the rate of decline in ovarian reserve. *Hum Reprod* 2013;**28**: 2140-2145.

Urman B, Alper E, Yakin K, Oktem O, Aksoy S, Alatas C, Mercan R, Ata B. Removal of unilateral endometriomas is associated with immediate and sustained reduction in ovarian reserve. *Reprod Biomed Online* 2013;**27**: 212-216.

Vercellini P, Chapron C, De Giorgi O, Consonni D, Frontino G, Crosignani PG. Coagulation or excision of ovarian endometriomas? *American journal of obstetrics and gynecology* 2003;**188**: 606-610.

Declaration

The authors report no financial or commercial conflicts of interest.

Figure legends

Figure 1: Multiplanar view showing an endometrioma with typical ground glass echogenicity (number 1) surrounded by growing follicles (numbers 2–7). The coloured lines mark the borders of the follicles and the endometrioma as identified by SonoAVC on the orthogonal planes.

Figure 2: Scatter plot showing change in endometrioma volume (Deltavolume in Y axis) across prestimulation endometrioma volume (V1 in X axis). Each dot represents one endometrioma. The unit of measurement is millilitres for both axis. Spearman's correlation coefficient 0.664; $P < 0.01$.

Table 1. Correlation between measures of ovarian response and change in endometrioma volume.[a]

ACCEPTED MANUSCRIPT

Measure of ovarian response	*Spearman's rho*
Number of follicles over 14 mm	–0.154
Serum oestradiol level on the day of trigger	–0.136
Number of cumulus oocyte complexes	–0.377

[a]None of the values are statistically significant.

Table 2. Baseline characteristics of the 25 women undergoing ovarian stimulation for IVF and outcome parameters.[a]

Characteristics	*Outcome*
Age	36.1 (4.6) years
Body mass index	22.9 (19.3–25.7) kg/m^2
Total antral follicle count	5 (3–8)
Serum anti-Müllerian hormone level	1.11 (0.7–1.83) ng/ml
Duration of stimulation	10.3 (2.3) days
Peak oestradiol level	1200 (821–2300) pg/ml
Number of cumulus oocyte complexes	5 (4–9)
Metaphase-two oocytes	4 (3 – 7)
Endometrioma volume on the first day of stimulation	22.2 ml (12–30 ml)
Endometrioma volume on the day of ovulation trigger	24.99 ml (11.2–37.4 ml)[b]
Live birth rate per fresh embryo transfer	42.9% (6/14)

[a]Figures are mean (SD) or median (25th to 75th percentile).
[b]Significantly different than endometrioma volume on the first day of stimulation; $P = 0.001$.

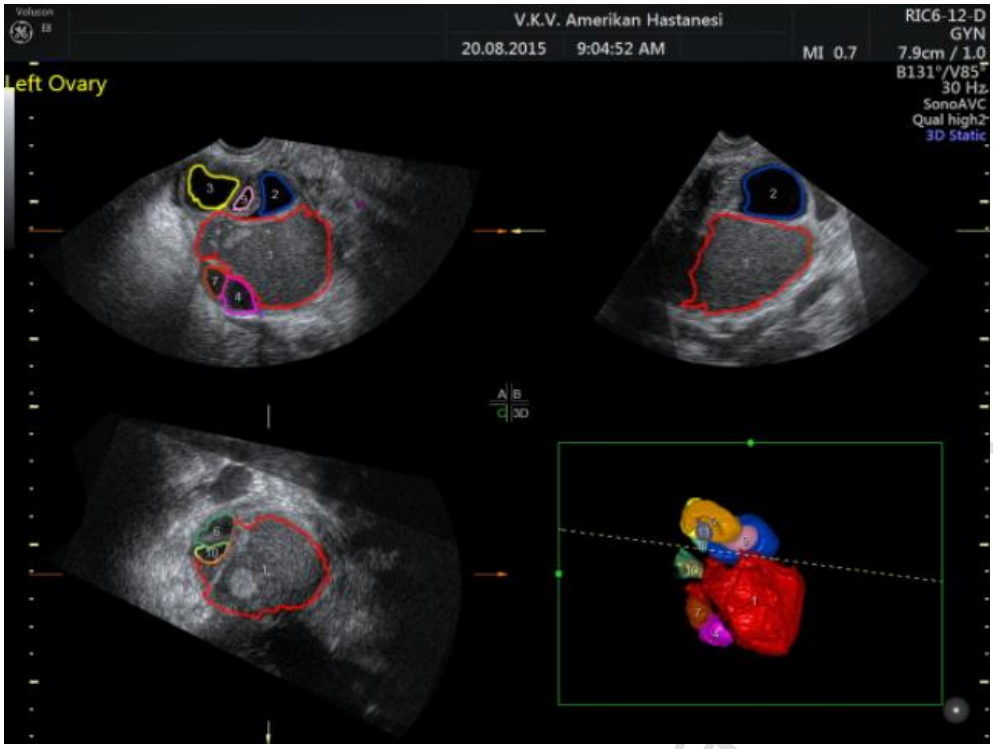
Accepted Manuscript

ACCEPTED MANUSCRIPT

ayse foto.jpg

Accepted Manuscript

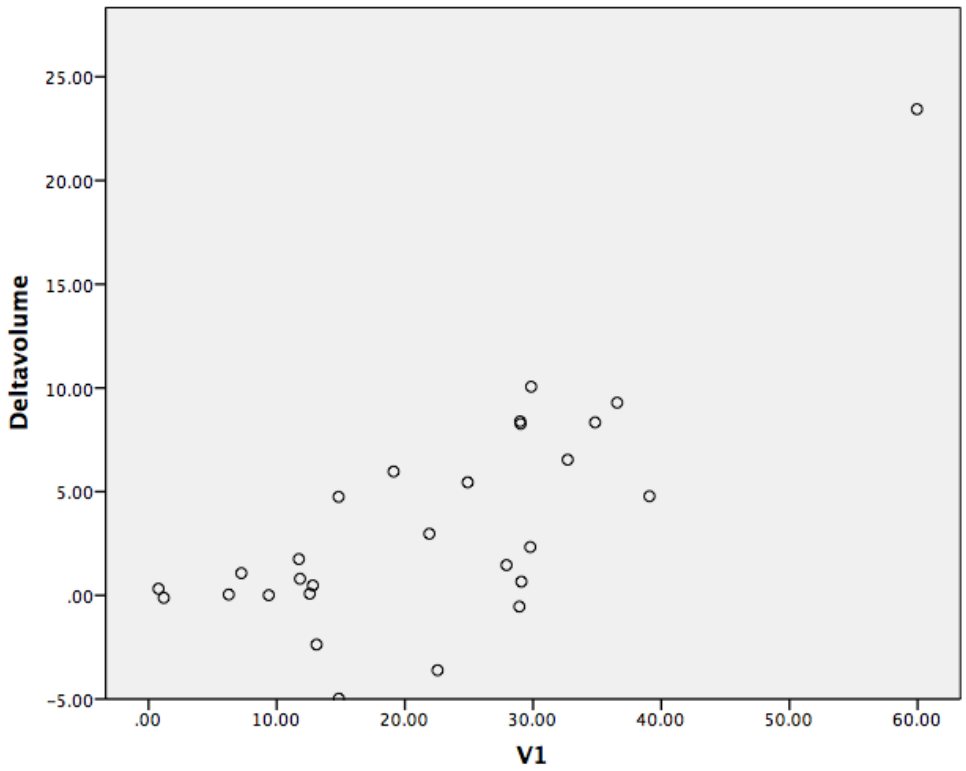
ACCEPTED MANUSCRIPT



Seyhan Figure 1_bestsetConverted.png

Accepted Manuscript

ACCEPTED MANUSCRIPT



Seyhan Figure 2_V2_bestsetConverted.png

Accepted M